

Green, Charles Velmar

1931. Size inheritance and growth in a mouse species
cross (*Mus musculus* × *Mus bactrianus*)

I. Litter size

Jour. Exp. Zool., v. 58, Jan. 5

Genetics, hybridization

Mouse

Litters, hybrid—factors determining size

THE WISTAR INSTITUTE PRESS
Philadelphia, Pa., U.S.A.

C.V. Green

111



SIZE INHERITANCE AND GROWTH IN A MOUSE SPECIES CROSS (MUS MUSCULUS $\times$ MUS BACTRIANUS)

I. LITTER SIZE¹

C. V. GREEN

Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine

TWO CHARTS

The class Mammalia exhibits wide variations in fecundity. Many of the rodents produce large litters at short intervals, while at the other extreme come such slow-breeding forms as the Proboscidea, which give birth to a single young at intervals of some years. Within a given genus the different species may show wide variation in litter size and even within a single species different races may show marked variability. Thus, within the limits of normal variation, the fecundity of a species or of a race is specifically or racially fixed as a specific or racial characteristic. These facts are clearly demonstrated by a comparison of the averages of large series of litters produced by females of the various stocks. The behavior of litter size in an interspecific cross is therefore a matter of interest.

The forms used in the present cross were a small, light-colored, white-bellied Asiatic mouse, *Mus bactrianus*, and the Little inbred strain of dilute brown non-agouti *Mus musculus*. The original animals of our *Mus bactrianus* stock were taken near Peiping, China, and brought to the United States by Dr. Sheo Nan Cheer in 1926. Dr. G. M. Allen has identified

¹ One of a series from a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Zoology of the University of Michigan.

specimens of our stock as intermediate between the Gobi Desert race, *Mus bactrianus gansuensis*, and the race occurring in western China, *Mus bactrianus tantillus*, although on the whole nearer the former. *Mus bactrianus* differs from our domesticated *Mus musculus* in many respects, such as the number of caudal vertebrae, peculiarities in the shape of the skull, relative tail length, color (the *bactrianus* animals are intense black agouti), and size.

Bactrianus males cross readily with *musculus* females and the offspring of both sexes are fertile. A number of litters from the reciprocal cross have also been obtained, although, perhaps because of the discrepancy in size (*bactrianus* weighing less than half as much as *musculus*), this cross is less readily made.

In addition to the inherent characteristics of a race, there are other factors which have been reported as affecting fecundity and litter size. Chief among these are nutritional deficiencies (Wright, '22, in guinea-pigs), alcohol (MacDowell, '21, '22, and Hanson and Heys, '27, in rats, and Crew, '25, in mice), epidemic diseases (Nelson, '09, in hares), age and weight of female, position of litter in the series, time of year, and hybridization.

The age and weight of the female seem sometimes to have a marked effect on the number of young produced per litter. King ('16) found that young and very old albino female rats had not only a greater variation in litter size, but actually smaller litters than females at the height of their reproductive activity. Feldman ('25, '26) also found the age of the female to be a factor in litter size, the younger rats having smaller litters than the average, whereas the smallest were in the most advanced age groups. In guinea-pigs Wright ('22) stated that the age of the dam has an influence on the size of the litter, but not an important one.

There also appears to be a slight positive correlation between weight of female and litter size, but, since weight is a function of age, it per se cannot be considered of primary importance in determining litter size.

King ('16) and King and Stotsenburg ('15) asserted that the position of the litter in the series had an effect on litter size; the second and third litters were larger than the first or fourth. Feldman ('25), likewise working with rats, stated that the position of a litter in the female's reproductive history was not in itself a factor for determining the number of live individuals in that litter.

The evidence concerning the influence of the time of year on litter size in rodents is also conflicting. King and Stotsenburg (*loc.cit.*) stated that there was no pronounced seasonal variation in the albino rat. Hanson and Sholes ('24) found some slight differences in the litter size of albino rats born at different seasons of the year, but none was great enough in respect to its probable error to be significant. Feldman ('26) found marked differences in the monthly averages. King ('27) stated that the average size of litters cast appeared to be fairly constant throughout the year. The average size, however, is somewhat greater during the first half of the year than during the second half. In some strains of rats the average was lowest in winter and highest in spring, while in others the minimum average occurred in summer.

There are scanty data in the literature regarding seasonal variation in litter size in the mouse. Parkes ('26) presented data showing that spring litters averaged smallest and autumn litters, largest. Bluhm ('29) found exactly the reverse, that litters were largest in spring and smallest in autumn. Her differences were likewise slight and do not alter the validity of the statement made by King ('27) that "there is little reason to suppose that litter size in the mouse is influenced to any marked degree by the season of the year in which conception occurs."

An increase in litter size, perhaps a manifestation of heterosis, often accompanies hybridization. This occurs not only in interspecific crosses, but also in matings between two inbred strains of the same species. Wright ('22 a) stated that the cross between an inbred male guinea-pig and a cross-bred female gave such a great increase in litter size that there

can be no question about the effect of cross-breeding of the dam on her fecundity. Detlefsen ('14) found, on the contrary, that female hybrids, produced by crossing a wild Brazilian cavy, *Cavia rufescens*, with the domestic guinea-pig, *Cavia porcellus*, had litters intermediate between the wild and tame races in size.

King ('27), in a summary of litter production in various strains of rats (*Rattus norvegicus*), presented data indicating that hybridization effected a slight increase in litter size.

A. C. and A. L. Hagedoorn ('28) crossed albino mice (*Mus musculus*) with a small oriental domestic mouse imported from Australia which they consider to be *Mus wagneri*. The average litter size of the Australian mice was 2.02, while that of the albinos was 5.5. The F_1 females gave a litter size of 5.0. Gates ('26) obtained litters averaging 4.6 young from Japanese waltzing mice, a race he considers to be derived from *Mus wagneri* (*Mus bactrianus*). His pink-eyed, dilute brown *Mus musculus* averaged 6.1 young per litter, while the litter size of the hybrids was 5.7. In both these instances the litter size of the hybrid approached that of the more fecund parent.

In order to determine the effect of the age of the female on litter size, 1362 litters of one of our parent stocks, dilute brown *Mus musculus*, born during the year 1928, were classified according to the age of the female at the time the litter was born. This distribution and the mean litter size for each of the age groups are shown in table 1. A very few litters born to females less than sixty-one days old are not included. Chart 1 presents graphically the relationship between age and litter size.

It will be seen that very young females give birth to small litters. The average size ascends rapidly until the maximum is attained at 150 days. With some fluctuations, perhaps chance deviations, litter size remains high until after 300 days. Although the curve has a semblance of bimodalism, a more likely interpretation seems to be that the curve of best fit is a second degree (parabolic) curve. Too much impor-

TABLE 1
Age and litter size in *Mus musculus* × *Mus musculus* matings

NUMBER IN LITTER	AGE IN DAYS																	
	61-80	81-100	101-120	121-140	141-160	161-180	181-200	201-220	221-240	241-260	261-280	281-300	301-320	321-340	341-360	361-380	381-	
1	4	5	4	3	2	5	2	4	5	4		1				1	1	41
2	21	13	12	8	4	7	1	4	3	4	2	2	3	1	2	1	1	88
3	18	26	16	9	7	10	11	5	5	12	6	6	1		2	2	1	137
4	21	37	27	14	10	14	11	11	11	10	10	8	4	4	4	4	4	200
5	14	37	34	32	25	18	14	11	17	12	10	9	5	3	2	1	1	245
6	25	36	26	21	23	21	22	16	16	5	14	10	3	6	6	1	3	254
7	5	25	16	22	24	9	9	17	15	10	8	8	5	3			1	177
8	1	14	18	11	13	15	19	14	4	3	8	3	2	1	1	1	1	129
9		5	4	3	11	9	6	7	2	4	1	1	1		1			56
10		2	4		3	9	1	2	2		1	1						25
11		1		1					1		1							6
12		1		1							1		2	1				4
Number of litters	109	202	161	125	123	117	96	91	81	64	61	49	26	20	14	11	12	1362
Mean litter size.	4.1	5.1	5.2	5.4	6.1	5.8	5.9	5.9	5.4	4.8	5.7	5.3	5.8	5.9	4.9	3.9	4.5	

tance must not be assigned to the fluctuations, since some of the numbers are small and they may be merely chance deviations of sampling. In this connection, Wright's ('22) statement that in guinea-pigs the age of the dam has no important influence on litter size may be recalled. Then, too, since all our stocks are comparable, none having an excess of very old or very young females, such effects as the maternal age may have on litter size probably do not greatly alter the validity of our averages.

Chart 2 shows the distribution of all the litters of dilute brown *Mus musculus* born during 1928. They range in size

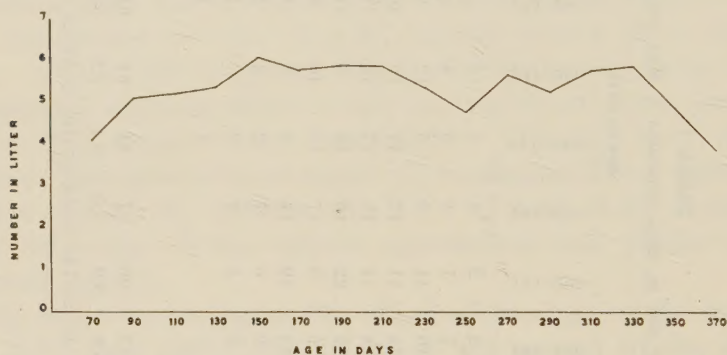


Chart 1 Litter size of *Mus musculus* according to age of mothers.

from one to twelve, with a mean for the 1400 litters of $5.4 \pm .04$. Stillbirths are included in this, as in all other litter-size calculations. This curve seems closely to approximate one of normal distribution.

In table 2 the litters are arranged according to time of year. There seem to be considerable—although no consistent—fluctuations in the different months. The averages vary from $4.8 \pm .14$ in March to $5.8 \pm .10$ in December. When presented by quarters, litters are shown to average largest in autumn ($5.7 \pm .07$) and smallest in spring ($5.1 \pm .08$). These findings agree with Parkes ('26), but disagree with Bluhm ('29), although she had more than 3000 litters. Our data also

show that litters are larger during the second half of the year than during the first half ($5.5 \pm .05$ and $5.2 \pm .06$). Since these results do not appear to be consistent and since litters in all our experimental stocks were born throughout the year, conclusions drawn from a study of averages are not invalidated.

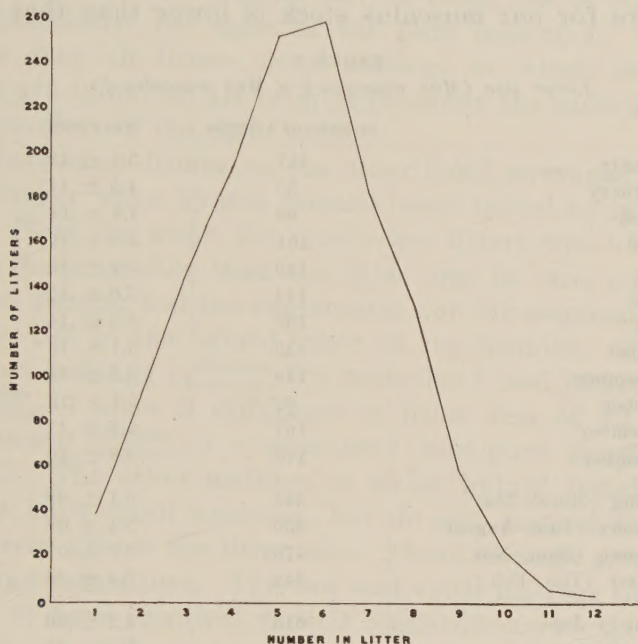


Chart 2 Litter size in *Mus musculus*.

The position of the litter in the series is usually rather closely correlated with the age of the mother, so, as has been pointed out by Feldman ('25), is not in itself a factor influencing litter size.

During the course of the experiment the diet and other environmental factors were kept constant, no known deleterious substances such as alcohol were administered, and there were no epidemics, so neither these factors nor the other variables already considered can seriously have affected the comparability of our data.

Table 3 gives a summary of the litter sizes for the pure matings as well as for the several types of hybrid matings in the study.

Straight musculus has a litter size of $5.4 \pm .04$, while that of pure bactrianus is $4.6 \pm .11$. The difference, $0.8 \pm .12$, is seven times its probable error and unquestionably significant. The figure for our musculus stock is lower than that given

TABLE 2
Litter size (Mus musculus ♀ × Mus musculus ♂)

	NUMBER OF LITTERS	MEAN SIZE
January	117	$5.1 \pm .13$
February	55	$4.9 \pm .17$
March	92	$4.8 \pm .14$
April	101	$5.0 \pm .12$
May	140	$5.4 \pm .13$
June	111	$5.6 \pm .13$
July	107	$5.5 \pm .14$
August	132	$5.1 \pm .12$
September	116	$5.5 \pm .14$
October	92	$5.7 \pm .13$
November	167	$5.5 \pm .11$
December	170	$5.8 \pm .10$
Spring (March-May)	333	$5.1 \pm .08$
Summer (June-August)	350	$5.4 \pm .08$
Autumn (Sept.-Nov.)	375	$5.7 \pm .07$
Winter (Dec.-Feb.)	342	$5.4 \pm .08$
January-June	616	$5.2 \pm .06$
July-December	784	$5.5 \pm .05$
Total for year	1400	$5.4 \pm .04$

TABLE 3
Summary of litter sizes

MATING	NUMBER OF LITTERS	MEAN
1. Musculus ♀ × musculus ♂	1400	$5.4 \pm .04$
2. Bactrianus ♀ × bactrianus ♂	111	$4.6 \pm .11$
3. Musculus ♀ × bactrianus ♂	72	$5.4 \pm .20$
4. Bactrianus ♀ × musculus ♂	13	5.0
5. Musculus ♀ × $\frac{\text{musculus}}{\text{bactrianus}}$ ♂	124	$5.3 \pm .14$
6. $\frac{\text{Musculus}}{\text{Bactrianus}}$ ♀ × musculus ♂	92	$6.4 \pm .12$
7. $\frac{\text{Musculus}}{\text{Bactrianus}}$ ♀ × $\frac{\text{musculus}}{\text{bactrianus}}$ ♂	15	6.5
8. $\frac{\text{Musculus}}{\text{Bactrianus}}$ ♀ × bactrianus ♂	7	7.3

by Gates ('25), who found the average litter size to be $7.4 \pm .14$. The F_1 litters from *musculus* ♀ × *bactrianus* ♂ have a mean of $5.4 \pm .20$, identical in size with our *musculus* litters. The reciprocal F_1 litters are unfortunately too few in number to be of much significance. The back-cross litters from *musculus* females × F_1 males have a mean size of $5.3 \pm .14$, again practically the same as for pure *musculus*. Thus it appears that all litters from matings in which *musculus* females are employed are of approximately the same average size regardless of the male parent.

The back-cross litters, on the other hand, averaged significantly larger when hybrid females were mated to *musculus* males. Here the mean for ninety-two litters was $6.4 \pm .12$. This is much greater than the litter size in even our pure *musculus* parent, and the explanation for the augmented size probably lies in the hybrid vigor of the females. The two back-cross matings ($\frac{\text{musculus}}{\text{bactrianus}}$ ♀ × *musculus* ♂ and *musculus* ♀ × $\frac{\text{musculus}}{\text{bactrianus}}$ ♂) show a difference in litter size of $1.1 \pm .18$; that between $\frac{\text{musculus}}{\text{bactrianus}}$ ♀ × *musculus* ♂ and pure *musculus* is $1.0 \pm .13$. The other matings in which hybrid females are involved have small numbers, but do not suggest that the male parent affects the litter size. These findings give some interesting indications. The two back-cross matings (5 and 6 in table 3) have identical genetic compositions, so the much larger litters of the one must be due to the hybridity of the female. These results indicate that, in interspecific crosses in mice, the size of the litter is determined wholly by the dam, as Wright ('22) found was the case in crosses between inbred races of guinea-pigs, and not, as Davenport ('20) concluded in the production of twins in humans, that the paternal inheritance is nearly as potent as the maternal.

CONCLUSIONS

1. Our strains of *Mus musculus* and *Mus bactrianus* exhibit characteristically different average litter sizes, $5.4 \pm .04$ and $4.6 \pm .11$, respectively.
2. Litter size in mice is determined wholly by the female.
3. Litter size is significantly augmented by cross-breeding in the mother.

BIBLIOGRAPHY

- ALLEN, G. M. 1927 Murid rodents from the Asiatic expeditions. *Am. Mus. Novitates*, 270.
- BLUHM, A. 1929 Über einige das Geburtsgewicht der Säugetiere beeinflussende Faktoren (nach Beobachtungen an *Mus musculus albinus*). *W. Roux' Archiv. f. Entwmech.*, Bd. 116, S. 348-381.
- CREW, F. A. E. 1925 An attempt to disturb the sex-ratio in the mouse by the continual administration of alcohol to the male parent. *Proc. Royal Physical Soc.*, vol. 21, pp. 89-96.
- DETLEFSEN, J. A. 1924 Genetic studies on a cavy species cross. *Carnegie Inst. Wash. Pub.* 205.
- FELDMAN, H. W. 1925 Fertility of the rat, *Mus norvegicus*. *Proc. Nat. Acad. Sci.*, vol. 11, pp. 718-721.
- 1926 Fertility and sterility in the Norway rat, *Mus norvegicus*. *Carnegie Inst. Wash. Pub.* 337, pp. 49-82.
- GATES, W. H. 1925 Litter size, birth weight, and early growth rate of mice (*Mus musculus*). *Anat. Rec.*, vol. 29, pp. 183-193.
- 1926 The Japanese waltzing mouse. *Carnegie Inst. Wash. Pub.* 337, pp. 83-138.
- HAGEDOORN, A. C. AND A. L. 1928 Some genetic factors which influence litter size and sterility in domestic mice (*Mus musculus* and *Mus wagneri*). *Zeitschr. f. ind. Abst. u. Vererb.*, Supplementband 2, S. 785-787.
- HANSON, F. B., AND HEYS, F. 1927 The effects of alcohol on birth weight and litter size in the albino rat. *Am. Nat.*, vol. 61, pp. 503-519.
- HANSON, F. B., AND SHOLES, F. N. 1924 Seasonal differences in sex-ratio, litter size and birth rate of the albino rat under uniform laboratory conditions. *Genetics*, vol. 9, pp. 363-367.
- KING, H. D. 1916 The relation of age to fertility in the rat. *Anat. Rec.*, vol. 11, pp. 269-287.
- 1927 Seasonal variations in fertility and in the sex ratio of mammals, with special reference to the rat. *W. Roux' Arch. f. Entwmech.*, Bd. 12, S. 61-111.
- KING, H. D., AND STOTSENBURG, J. M. 1915 On the normal sex ratio and size of the litter in the albino rat. *Anat. Rec.*, vol. 9, pp. 403-419.
- MACDOWELL, E. C. 1921 Alcohol and white rats: a study of fertility. *Proc. Soc. Exp. Biol. and Med.*, vol. 19, pp. 69-71.
- 1922 The influence of alcohol on the fertility of white rats. *Genetics*, vol. 7, pp. 117-141.
- NELSON, E. W. 1909 The rabbits of North America. *North Am. Fauna*, no. 29.
- PARKES, A. S. 1926 The growth of young mice according to the size of litter. *Ann. Applied Biol.*, vol. 13, pp. 374-394.
- WRIGHT, S. 1922 The effects of inbreeding and crossbreeding on guinea pigs. I. Decline in vigor. II. Differentiation among inbred families. *U. S. Dept. Agr. Bull.* 1090, pp. 1-63.
- 1922 a The effects of inbreeding and crossbreeding on guinea pigs. III. Crosses between highly inbred families. *U. S. Dept. Agr. Bull.* 1121, pp. 1-60.

